Remarks

This is in response to the Official Action of February 1, 2005.

Claims 1-10 stand rejected as lacking utility under 35 USC 101, it being alleged that a "real world" utility for a mouse comprising an endogenous iNOS gene and a transgene encoding a human iNOS gene would not be apparent to the skilled artisan.

Applicants respectfully disagree. The skilled artisan, as of the July 21, 1998 priority date of the instant application, would have readily understood the utility of the claimed invention in light of the teaching of the specification and **long-established and widespread** public knowledge regarding the iNOS as a target for drug treatment. Consideration of the following evidence is respectfully requested.

US Patent No. 5,266,594 to Dawson et al., Inhibitors of nitric oxide synthase and use thereof to prevent glutamate neurotoxicity (Issued November 30, 1993) recites as claim 1:

> 1. A method of preventing or treating a disease condition caused by glutamate neurotoxicity in a mammal comprising:
> administering to a mammal in need thereof a therapeutically effective amount of an inhibitor of ***nitric oxide*** synthase.

US Patent No. 5,674,907 to Southan et al., Mercapto derivatives as inhibitors of nitric oxide synthase (Issued October 7, 1997) (Children's Hospital Medical Center, Cincinnati, OH), recites as claim 1:

> 1. A method for inhibiting ***nitric oxide*** synthase in a mammal comprising: administering to the mammal an effective amount of a mercapto derivative to inhibit ***nitric oxide*** synthase in the mammal, said mercapto derivative having the formula....

US Patent No. 5,741,815 to Lai, Methods for in vivo reduction of nitric oxide levels and compositions useful therefor (Issued April 21, 1998), recites as claims 1 and 2:

> 1. A method for the in vivo reduction of ***nitric oxide*** levels in a subject, said method comprising:
> administering to said subject an effective amount of at least one dithiocarbamate-containing ***nitric oxide*** scavenger, wherein said dithiocarbamate-containing ***nitric oxide*** scavenger comprises a dithiocarbamate moiety and, optionally

a physiologically compatible di- or tri-valent transition metal ion, wherein said dithiocarbamate has the structure....

2. A method for treating ***nitric oxide*** overproduction in a subject, said method comprising

administering to said subject an effective amount of at least one dithiocarbamate-containing ***nitric oxide*** scavenger, wherein said dithiocarbamate-containing ***nitric oxide*** scavenger comprises a dithiocarbamate moiety and, optionally, a physiologically compatible di- or tri-valent transition metal ion, wherein said dithiocarbamate has the structure....

US Patent No. 5,756,540 to Lai, Methods for in vivo reduction of nitric oxide levels and compositions useful therefor (Issued May 26, 1998) (assigned to MCW Research Foundation, Inc), recites as claims 1 and 2 the following:

1. A method for the in vivo reduction of ***nitric oxide*** levels in a subject, said method comprising:

administering to said subject an effective amount of at least one dithiocarbamate-containing ***nitric oxide*** scavenger.

2. A method for treating ***nitric oxide*** overproduction in a subject, said method comprising:

administering to said subject an effective amount of at least one dithiocarbamate-containing ***nitric oxide*** scavenger.

US Patent No. 5,902,810 to Pfleiderer et al., Pteridine derivatives as no synthase inhibitors (Issued May 11, 1999, based upon a PCT Application published November 30, 1995 and a German priority document filed May 24, 1994) (assigned to Hoechst) recites as claim 1:

1. A method for the treatment of a disease associated with an increased ***nitric oxide*** level which comprises administering to a mammal in need of such treatment an effective amount of a pteridine derivative of the formula.....

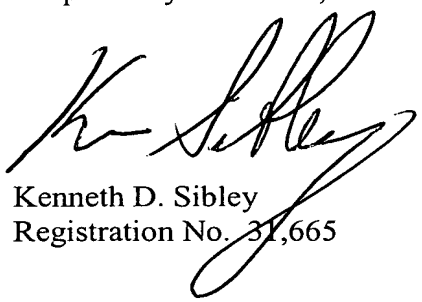
Skilled persons, knowing of the long-established role of nitric oxide in disease, would have readily understood how to use animals of the present invention in investigating these, and other, compounds for the treatment of disease. Accordingly, it is respectfully submitted that

this applications meets the utility requirement under 35 USC 101, and respectfully submitted that this rejection should be withdrawn.

Claims 1 and 3-10 are further rejected as lacking enablement under 35 USC 112, first paragraph, it being alleged that at the time of filing the skilled artisan would not have regarded the claimed mouse or methods as having an enabled use. It is respectfully submitted that this rejection is obviated for the same reasons set forth above, and respectfully submitted that this rejection should be withdrawn.

It is respectfully submitted that this application is in condition for allowance, which action is respectfully requested.

Respectfully submitted,



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